REMARKS

Claims 17-31 currently appear in this application. The Office Action of January 11, 2008, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Rejections under 35 U.S.C. 112

Claims 17-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification is said not to provide enablement for prevention of the diseases claimed.

This rejection is respectfully traversed. Claim 17 has been amended to delete prevention. Since claims 18-31 depend from claim 17, this amendment should obviate the rejection with respect to claims 17-31.

Claim Objections

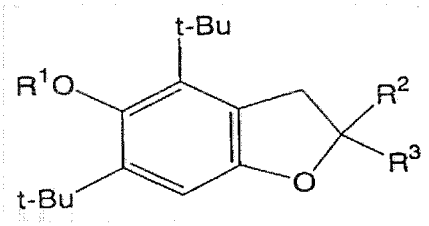
Claims 18-31 are objected to under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claims 18-31 have now been amended to recite a method rather than a composition.

Art Rejections

Claims 17-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tamura et al., US 5,574,178 in view of Tsujii et al., US 5,043,354.

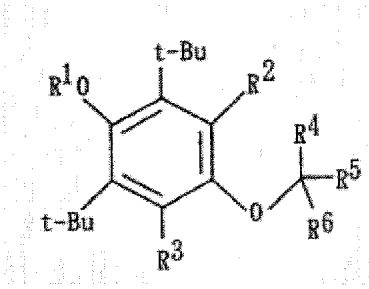
This rejection is respectfully traversed. The present claims are drawn to a method for treating fatty liver or hepatic diseases by administering a compound of formula (1)



(1)

Test Example 1 in the present specification, pages 15-20, demonstrates the effectiveness of these compounds for treating fatty liver or hepatic diseases.

Tamura discloses a compound of formula (I):

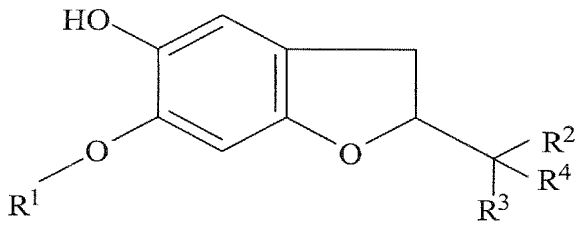


(I)

The Tamura compound has a highly selective antioxidant activity and is useful for therapeutics for ischemic disease. There is neither disclosure nor suggestion in Tamura for treating fatty liver or hepatic diseases.

Tsujii disclose that a benzofuran derivative of the formula:

(I)



has an activity including scavenging reactive oxygen species and organic radicals. The compounds disclosed are said to be useful for treating ischemic diseases and liver disorders. This disclosure is said to suggest that the antioxidative properties are responsible for the usefulness of this drug in treating hepatic disorders.

There are no data in Tsujii demonstrating the use of the benzofuran derivatives for treating liver disorders. In this respect, there are several reports which contraindicate such use.

For example, Prince et al., *Aliment. Pharmacol. Ther.*, 2003 **17**:137-145 describes in the passage titled "Conclusions" at page 173, right column, that, although oral

antioxidant supplementation appears to be safe, the authors could not find any evidence for a beneficial effect on fatigue or other liver-related symptoms. Houglum et al., *Gastroenterology*, 1997 **113**:1069-1073, describes in the paragraph titled "Background & Aims" appearing on page 1069, left column, that eight weeks of d-α-tocopherol treatment did not significantly affect serum alanine aminotransferase levels, hepatitis C virus titers, or histological degree of hepatocellular inflammation or fibrosis. It should be noted that d-α-tocopherol is an antioxidant, as indicated in the same paragraph. These reports are referred to in the present specification.

Gunduz et al., *J. Gastroenterol*.2003 **9(12)**:2698-2700, describe in the paragraph entitled "Conclusion" appearing at page 2698, left column, that NAC administration affected neither the time necessary for normalization of SLT and total bilirubin values nor duration of hospitalization, so that the authors would not recommend NAC for treating icteric AVH cases. NAC is N-acetyl cysteine, which is a reducing agent, *i.e.*, has antioxidative activity, as described on page 2698, right column, lines 6-9. AVH is acute viral hepatitis. A copy of this article is submitted herewith.

Mezey et al., *J. Hepatol*, 2004 **40(1)**:40-46, describe in the paragraph titled "Conclusions" appearing on page 40,

that vitamin E treatment improves serum hyaluronic acid but has not beneficial effect on tests of liver function in patients with mild to moderate alcoholic hepatitis. It is noted that vitamin E acts as an antioxidant and comprises a number of tocopherol isomers, as described at page 40, right columns, lines 2-7. A copy of this article is submitted herewith.

Collectively considering the absence of data demonstrating the usefulness of the benzofuran derivative for treating liver disorders and the descriptions in the reports mentioned immediately above, it is respectfully submitted that the Tsujii suggestion of treating liver disorders is unreliable.

Further, the compound disclosed in Tamura is significantly different in structure from the benzofuran derivative disclosed in Tsujii. Specifically, while the Tamura compound has at least two t-Bu groups on the phenol ring, the Tsujii has no t-Bu group but, instead, has an ether group, R^1-O-, on the phenol ring. Indeed, the phenol ring of the benzofuran derivative in Tsujii should more precisely be referred to as the "catechol ring."

In view of the unreliability of the suggestion in Tsujii that the compounds treat liver diseases, and the differences in structure between the compounds of Tsujii and

Tamura, it is respectfully submitted that one skilled in the art would not have expected that the Tamura compound would be useful for treating liver disorders. In this connection, the data entitled "P+ high fat diet" shown in Table 2 provided in the present specification shows that the Probucul (referred to as "P" in Table 1), which has phenol rings each having two t-Bu groups and an antioxidative activity, as is the case in the Tamura compound, was ineffective in treating fatty liver and associated hepatic disease. The structure of Probucul is shown on page 3083, right column, of *J.Med. Chem.* 2003, (46):3083-3093, a copy of which is submitted herewith. This article notes that Probucol has antioxidative activity, page 3083, left column, line 14. Further, d-α-tocopherol, which is closer to the compound disclosed in Tamura than the benzofuran derivative disclosed in Tsujii in that it is an antioxidant and its phenol ring has two alkyl groups adjacent to the phenolic hydroxyl groups, is described in Houglum et al. *supra*, as not significantly affecting hepatitis C virus titers or histological degree of hepatocellular inflammation, right column, page 3083. These facts support the unexpectedness of the usefulness of the compounds disclosed in Tamura for treatment of disorders of the liver.

Therefore, one skilled in the art would not have expected from the disclosures of Tamura and Tsujii that the

compound of claim 17, which is disclosed in Tamura, could be used for treating fatty liver or hepatic diseases. Accordingly, claims 17-31 are not obvious over Tamura in view of Tsujii.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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